DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
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March 7, 2016

CEPHEID
JIM KELLY, Ph.D.
EXECUTIVE DIRECTOR, REGULATORY AFFAIRS
904 CARIBBEAN DRIVE
SUNNYVALE CA 94089-1189

Re: K152614
Trade/Device Name: Xpert® Carba-R
Regulation Number: 21 CFR 866.1640
Regulation Name: Antimicrobial susceptibility test powder
Regulatory Class: II
Product Code: PMY, OOI
Dated: February 5, 2016
Received: February 8, 2016

Dear Dr. Kelly:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Ribhi Shawar -S

For Uwe Scherf, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of *In Vitro* Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*

K152614

Device Name

Xpert Carba-R

Indications for Use *(Describe)*

The Xpert® Carba-R Assay, performed on the GeneXpert® Instrument Systems, is a qualitative *in vitro* diagnostic test for the detection and differentiation of the *bla*$_{KPC}$, *bla*$_{NDM}$, *bla*$_{VIM}$, *bla*$_{OXA-48}$, and *bla*$_{IMP}$ gene sequences associated with carbapenem-non-susceptible pure colonies of *Enterobacteriaceae*, *Acinetobacter baumannii*, or *Pseudomonas aeruginosa* grown on blood agar or MacConkey agar. The test utilizes automated real-time polymerase chain reaction (PCR).

A negative Xpert Carba-R Assay result does not preclude the presence of other resistance mechanisms. The Xpert Carba-R Assay should be used in conjunction with other laboratory tests including phenotypic antimicrobial susceptibility testing. The Xpert Carba-R Assay is intended as an aid for infection control in detecting and differentiating genetic markers of resistance to monitor the spread of carbapenem-non-susceptible organisms in healthcare settings. The Xpert Carba-R Assay is not intended to guide or monitor treatment for carbapenem-non-susceptible bacterial infections.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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510(k) Summary

As required by 21 CFR Section 807.92(c).

Submitted by:	Cepheid 904 Caribbean Drive Sunnyvale, CA 90489 Phone number: (847) 228-3299 Fax number: (847) 890-6589
Contact:	Scott A. Campbell, PhD, MBA
Date of Preparation:	March 2, 2016
Device:	
510(k) Number:	K152614
Trade name:	Xpert® Carba-R
Common name:	Xpert Carba-R Assay
Type of Test:	Qualitative nucleic acid amplification test of the *bla*$_{KPC}$, *bla*$_{NDM}$, *bla*$_{VIM}$, *bla*$_{OXA-48}$, and *bla*$_{IMP}$ gene sequences from isolates of pure cultures of carbapenem-non-susceptibility gram-negative bacteria
Classification:	II
Regulation number	866.1640
Classification name:	Antimicrobial susceptibility test powder
Product code:	PMY, OOI
Classification Advisory Panel	Microbiology (83)
Prescription Use	Yes
Predicate Device Assay:	Cepheid Xpert ® *vanA* [510(k) #K092953]

Device Description:

The Xpert Carba-R Assay is an automated real-time polymerase chain reaction (PCR) *in vitro* diagnostic test for qualitative detection of the *bla*$_{KPC}$, *bla*$_{NDM}$, *bla*$_{VIM}$, *bla*$_{OXA-48}$, and *bla*$_{IMP}$ gene sequences from isolates of pure cultures of carbapenem-non-susceptibility gram-negative bacteria. The Xpert Carba-R Assay is intended as an aid for infection control for monitoring the spread of carbapenem-non-susceptible organisms in healthcare settings.

The Xpert Carba-R Assay is performed on the Cepheid GeneXpert® Instrument Systems (GeneXpert Dx, GeneXpert Infinity-48, GeneXpert Infinity-48s, and GeneXpert Infinity-80 systems). The GeneXpert Instrument System platform automates sample preparation, amplification and real-time detection.

The GeneXpert Instrument Systems require the use of single-use, disposable cartridges (the Xpert Carba-R cartridges) that hold the PCR reagents and host the PCR process. Because the cartridges are self-contained and specimens never come into contact with working parts of the instrument modules, cross-contamination between samples is minimized.

The Xpert Carba-R Assay cartridges contain reagents for the detection of *bla*$_{KPC}$, *bla*$_{NDM}$, *bla*$_{VIM}$, *bla*$_{OXA-48}$, and *bla*$_{IMP}$ gene sequences. A Sample Processing Control (SPC) and a Probe Check Control (PCC) are controls utilized by the GeneXpert Instrument System platform. The SPC is present to control for adequate processing of the target bacteria and to monitor the presence of inhibitors in the real-time PCR reaction to reduce the possibility of false negative results. The PCC verifies reagent rehydration, real-time PCR tube filling in the cartridge, probe integrity, and dye stability.

The single-use, multi-chambered fluidic cartridges are designed to complete sample preparation and real-time PCR for the detection of the *bla*$_{KPC}$, *bla*$_{NDM}$, *bla*$_{VIM}$, *bla*$_{OXA-48}$, and *bla*$_{IMP}$ gene sequences from isolates of pure cultures of carbapenem-non-susceptibility gram-negative bacteria in approximately 50 minutes. The GeneXpert Instrument Systems, comprised of the GeneXpert Dx Systems and the GeneXpert Infinity Systems, have 1 to 80 randomly accessible modules, depending upon the instrument, that are each capable of performing separate sample processing and real-time PCR and RT-PCR tests. Each module contains a syringe drive for dispensing fluids (i.e., the syringe drive activates the plunger that works in concert with the rotary valve in the cartridge to move fluids between chambers), an ultrasonic horn for lysing cells or spores, and a proprietary I-CORE® thermocycler for performing real-time PCR and RT-PCR and detection.

The bacterial isolates from culture are placed into a sample reagent. The sample is transferred to the sample chamber of the disposable fluidic cartridge (the Xpert Carba-R cartridge). The user initiates a test from the system user interface and places the cartridge into the GeneXpert instrument platform, which performs hands-off real-time, multiplex PCR for detection of the *bla*$_{KPC}$, *bla*$_{NDM}$, *bla*$_{VIM}$, *bla*$_{OXA-48}$, and *bla*$_{IMP}$ gene sequences. The results are automatically generated at the end of the process in a report that can be viewed and printed.

Device Intended Use:

The Xpert® Carba-R Assay, performed on the GeneXpert® Instrument Systems, is a qualitative *in vitro* diagnostic test for the detection and differentiation of the bla_{KPC}, bla_{NDM}, bla_{VIM}, bla_{OXA-48}, and bla_{IMP} gene sequences associated with carbapenem-non-susceptible pure colonies of *Enterobacteriaceae, Acinetobacter baumannii*, or *Pseudomonas aeruginosa* grown on blood agar or MacConkey agar. The test utilizes automated real-time polymerase chain reaction (PCR).

A negative Xpert Carba-R Assay result does not preclude the presence of other resistance mechanisms. The Xpert Carba-R Assay should be used in conjunction with other laboratory tests including phenotypic antimicrobial susceptibility testing. The Xpert Carba-R Assay is intended as an aid for infection control in detecting and differentiating genetic markers of resistance to monitor the spread of carbapenem-non-susceptible organisms in healthcare settings. The Xpert Carba-R Assay is not intended to guide or monitor treatment for carbapenem-non-susceptible bacterial infections.

Substantial Equivalence:

The Cepheid Xpert Carba-R Assay is substantially equivalent to the Xpert® *vanA*, 510(k) #K092953. The Xpert Carba-R Assay and the Xpert *vanA* Assay both detect target gene sequences from antibiotic-resistant bacteria and use real-time PCR amplification and fluorogenic target-specific hybridization detection. The performance of the Xpert Carba-R Assay was determined in a multi-site clinical study in which the performance of the Xpert Carba-R Assay was evaluated relative to reference DNA sequence analysis. The results of the study demonstrated that the performance of the Xpert Carba-R Assay is substantially equivalent to the predicate device.

Table 5-1 shows the similarities and differences between the Xpert Carba-R Assay and the predicate device.

Table 5-1: Comparison of Similarities and Differences of the Xpert Carba-R Assay with the Predicate Device

Similarities		
Item	**Device**	**Predicate Device**
	Cepheid Xpert Carba-R Assay	**Cepheid Xpert *vanA* Assay K092953**
General Intended Use	The Xpert® Carba-R Assay, performed on the GeneXpert® Instrument Systems, is a qualitative *in vitro* diagnostic test for the **detection** and differentiation of the bla_{KPC}, bla_{NDM}, bla_{VIM}, bla_{OXA-48}, and bla_{IMP} **gene sequences** associated with carbapenem-non-susceptible pure colonies of *Enterobacteriaceae*, *Acinetobacter baumannii*, or *Pseudomonas aeruginosa* grown on blood agar or MacConkey agar. **The test utilizes automated real-time polymerase chain reaction (PCR).** A negative Xpert Carba-R Assay result does not preclude the presence of other resistance mechanisms. The Xpert® Carba-R Assay should be used in conjunction with other laboratory tests including phenotypic antimicrobial susceptibility testing. The Xpert Carba-R Assay is intended as an aid for infection control in detecting and differentiating genetic markers of resistance to monitor the spread of carbapenem-non-susceptible organisms in healthcare settings. The Xpert Carba-R Assay is not intended to guide or monitor treatment for carbapenem-non-susceptible bacterial infections.	The Cepheid Xpert® *vanA* Assay performed in the GeneXpert® Dx System is a qualitative *in vitro* diagnostic test designed for rapid **detection** of the *vanA* **gene sequence** associated with vancomycin resistance in bacteria obtained from rectal swab specimens from patients at risk for intestinal colonization with vancomycin-resistant **bacteria**. **The test utilizes automated real-time polymerase chain reaction (PCR**) to detect the *vanA* gene that is frequently associated with vancomycin-resistant *enterococci* (VRE). The Xpert *vanA* Assay is intended to aid in the recognition, prevention, and control of vancomycin resistant organisms that colonize patients in healthcare settings. The Xpert *vanA* Assay is not intended to diagnose infections caused by vancomycin-resistant bacteria nor to guide or monitor treatment for vancomycin-resistant bacterial infections. Concomitant cultures are necessary to recover organisms for confirmatory identification of vancomycin-resistant bacteria, antimicrobial susceptibility testing, and for epidemiological typing.

Similarities		
Item	**Device**	**Predicate Device**
	Cepheid Xpert Carba-R Assay	**Cepheid Xpert *vanA* Assay K092953**
Type of test	Same	Qualitative
Technological Principles	Same	Fully-automated nucleic acid amplification (DNA); real-time PCR
Test Cartridge	Same	Disposable single-use, multi-chambered fluidic cartridge
Probes	Same	TaqMan® Probes
Controls	Same	Internal sample processing control (SPC) and probe check control (PCC) External controls available
Instrument System	GeneXpert Instrument System (includes **GeneXpert Dx**, Infinity-48, Infinity-48s, and Infinity-80)	**GeneXpert Dx**
Time to obtain test results	Approximately 50 minutes to results	Approximately 45 minutes to results
Interpretation of test results	**Diagnostic software** of the GeneXpert Instrument System	**Diagnostic software** of the GeneXpert Dx
Laboratory Users	Operators in CLIA Moderate or High Complexity labs	Operators in CLIA Moderate or High Complexity labs
Differences		
	New Device	**Predicate Device**
Item	**Cepheid Xpert Carba-R Assay**	**Cepheid Xpert *vanA* Assay K092953**
Sample Type	Bacterial isolates from culture	Rectal swabs
Assay Targets	Detects bla_{KPC}, bla_{NDM}, bla_{VIM}, bla_{OXA-48}, and bla_{IMP} gene sequences	Detects gene sequences for the *vanA* encoded resistance to vancomycin/teicoplanin

Similarities		
Item	**Device**	**Predicate Device**
	Cepheid Xpert Carba-R Assay	**Cepheid Xpert *vanA* Assay K092953**
Instrument System	GeneXpert Instrument System (includes GeneXpert Dx, **Infinity-48, Infinity-48s, and Infinity-80**)	GeneXpert Dx

The Xpert Carba-R Assay has the same general intended use as the predicate device and has the same technological characteristics as the predicate device. The differences between the Xpert Carba-R Assay and the predicate device do not raise questions of safety and effectiveness. The clinical study demonstrates that the Xpert Carba-R Assay is acceptable for its intended use with inexperienced laboratory users and is substantially equivalent to the predicate device described above.

Non-Clinical Studies:

Analytical Reactivity (Inclusivity)

The analytical sensitivity of the Xpert Carba-R Assay was evaluated by testing a panel of 71 samples consisting of 11 *bla*$_{KPC}$ (KPC), 13 *bla*$_{NDM}$ (NDM), 11 *bla*$_{VIM}$ (VIM), 8 *bla*$_{OXA-48}$ (OXA-48), 5 *bla*$_{NDM/OXA-181}$ (NDM/OXA-181), 5 *bla*$_{OXA-181}$ (OXA-181), 17 *bla*$_{IMP}$ (IMP), and one *bla*$_{KPC/VIM}$ (KPC/VIM) well-characterized bacterial strains (Table 5-2). Organisms were tested in replicates of four that were prepared by diluting 10 µL of 0.5 McFarland cell suspension for each bacterial strain in 5 mL of Xpert Carba-R Sample Reagent. Testing was performed using both blood agar and MacConkey plates. Xpert Carba-R Assay target genes were detected in 68 of 71 bacterial strains from both plates (Table 5-2). Xpert Carba-R Assay target DNA sequences were not detected in three bacterial strains as shown in Table 5-2. In one of the three bacterial strains, the IMP-13 gene was not detected by the assay, although it was predicted to be detected by *in silico* analysis. In two of the three bacterial strains, theIMP-7 and IMP-14 genes that were not detected by the assay were also not predicted to be detected by *in silico* analysis. See the Limitations section in the package insert.

The variants detected, and predictions for detecting other subtypes of each resistance gene based on *in silico* analysis, are presented in Table 5-3.

Table 5-2: Analytical Reactivity of the Xpert Carba-R Assay

Strain ID	Organism	Resistance Marker with variant information
NCTC 13438	*Klebsiella pneumoniae*	KPC-3
31551	*Klebsiella pneumoniae*	KPC-4
ATCC BAA-1705	*Klebsiella pneumoniae*	KPC-2
CFVL	*Enterobacter cloacae*	KPC-2
KBM18	*Enterobacter aerogenes*	KPC-2
COL	*Escherichia coli*	KPC-2
BM9	*Klebsiella pneumoniae*	KPC-3
CGNC	*Serratia marcescens*	KPC-2
PA3	*Pseudomonas aeruginosa*	KPC-2
COL	*Pseudomonas aeruginosa*	KPC-2
GR-04/KP-69	*Klebsiella pneumoniae*	KPC-2, VIM
164-3	*Klebsiella oxytoca*	KPC
NCTC 13437	*Pseudomonas aeruginosa*	VIM-10
NCTC 13439	*Klebsiella pneumoniae*	VIM-1
NCTC 13440	*Klebsiella pneumoniae*	VIM-1
758	*Pseudomonas aeruginosa*	VIM
N/A	*Klebsiella pneumoniae*	VIM
N/A	*Pseudomonas aeruginosa*	VIM
Col1	*Pseudomonas aeruginosa*	VIM-2
BM19	*Serratia marcescens*	VIM-2
KOW7	*Escherichia coli*	VIM-4
DIH	*Klebsiella pneumoniae*	VIM-19
MSH2014-3	*Enterobacter cloacae*	VIM
NCTC 13443	*Klebsiella pneumoniae*	NDM-1
ATCC BAA-2146	*Klebsiella pneumoniae*	NDM-1
34262	*Klebsiella pneumoniae*	NDM
GEN	*Acinetobacter baumannii*	NDM-1
3047	*Enterobacter cloacae*	NDM-1
7892	*Proteus mirabilis*	NDM-1
CAN	*Salmonella spp.*	NDM-1
EGY	*Acinetobacter baumannii*	NDM-2
I5	*Escherichia coli*	NDM-4
405	*Escherichia coli*	NDM-5
CF-ABE	*Citrobacter freundii*	NDM
73999	*Pseudomonas aeruginosa*	NDM
39365	*Providencia rettgeri*	NDM-1

Strain ID	Organism	Resistance Marker with variant information
NCTC 13442	*Klebsiella pneumoniae*	OXA-48
OM11	*Klebsiella pneumoniae*	OXA-48
501	*Enterobacter cloacae*	OXA-48
DUW	*Klebsiella pneumoniae*	OXA-48
OM22	*Escherichia coli*	OXA-48
BOU	*Enterobacter cloacae*	OXA-48
TUR	*Enterobacter cloacae*	OXA-48
11670	*Escherichia coli*	OXA-48
MSH2014-64	*Klebsiella pneumoniae*	OXA-181
MSH2014-72	*Escherichia coli*	OXA-181
B108A	*Klebsiella pneumoniae*	NDM, OXA-181
C10192-DISCS	*Enterobacter aerogenes*	NDM, OXA-181
KP-OMA3	*Klebsiella pneumoniae*	NDM-1, OXA-181
166643	*Klebsiella pneumoniae*	OXA-181
42194	*Klebsiella pneumoniae*	OXA-181
1300920	*Klebsiella pneumoniae*	NDM, OXA-181
MSH2014-69	*Klebsiella pneumoniae*	NDM, OXA-181
74	*Escherichia coli*	OXA-181
NCTC 13476	*Escherichia coli*	IMP-1
695	*Acinetobacter baumannii*	IMP-1
2340	*Enterobacter cloacae*	IMP-1
IMPBMI	*Klebsiella pneumoniae*	IMP-1
6852	*Klebsiella pneumoniae*	IMP-1
Yonsei_1	*Acinetobacter baumannii*	IMP-1
Yonsei_2	*Acinetobacter baumannii*	IMP-1
70450-1	*Pseudomonas aeruginosa*	IMP-1
3994	*Pseudomonas*	IMP-10
MKAM	*Pseudomonas aeruginosa*	IMP-1
5344	*Pseudomonas aeruginosa*	IMP-2
G029	*Salmonella spp*	IMP-4
3985	*Pseudomonas aeruginosa*	IMP-11
4032	*Pseudomonas aeruginosa*	IMP-6
3424	*Pseudomonas aeruginosa*	IMP-7 [a,b]
32443	*Klebsiella pneumoniae*	IMP-13 [a]
92	*Pseudomonas aeruginosa*	IMP-14 [a, b]

a. Not detected by Xpert Carba-R (see Limitations in package insert).

b. IMP-7 and IMP-14 genes were not detected by the assay and were not predicted to be detected by *in silico* analysis (see Limitations in package insert).

Table 5-3: Summary of Variants Detected by Wet Testing or Predicted to be Detected Based on *In Silico* Analysis

Marker (or Traditional Subgroup)	Wet testing			Not tested but predicted to be detected based on *in silico* analysis
	No. of Samples	Type(s) Detected	Type(s) not Detected	
KPC	12	KPC-2, 3, 4	--	KPC-5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16
NDM	18	NDM-1, 2, 4, 5	--	NDM-3, 6, 7, 8, 9
VIM	12	VIM-1, 2, 4, 10, 19	--	VIM-5, 6, 7, 8, 9, 11, 12, 13, 14, 15, 16, 17, 18, 20, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38
OXA-48	18	OXA-48, 181(OXA-48 variant)	--	OXA-162, 163, 204, 232, 244, 245, 247
IMP	17	IMP-1 (9 strains), IMP-2, 4, 6, 10, 11	IMP-7[a], 13[b], 14[a]	IMP-3, 8, 9, 13[b], 19, 20, 21, 22, 24, 25, 27, 28, 30, 31, 33, 37, 40, 42

a. IMP-7 and IMP-14 genes (*Pseudomonas aeruginosa*) were not detected by the assay and were not predicted to be detected by *in silico* analysis (see Limitations in package insert).
b. IMP-13 gene (*Klebsiella pneumoniae*): although predicted to be detected by *in silico* analysis, the IMP-13 gene was not detected by the assay (see Limitations in package insert).

Analytical Specificity (Cross-reactivity)

The analytical specificity of the Xpert Carba-R Assay was evaluated by testing a panel of 62 well-characterized bacterial strains of carbapenem-susceptible bacteria or bacteria with carbapenem non-susceptibility due to genes or mechanisms other than the Xpert Carba-R target genes (Table 5-4 and Table 5-5). Twenty-four commensal bacterial strains and other enteric microorganisms were also evaluated in the study (Table 5-6). Resistance mechanisms were determined by individual PCR assays, DNA sequence analysis, or Check-Points array version CT102.

Organisms were grown aerobically on blood agar and MacConkey agar plates or chocolate agar plates. Two cell suspensions equivalent to a 0.5 McFarland cell suspension were prepared from isolated colonies on each type of agar plate. Each organism was tested a total of four times (two replicates from each of two 0.5 McFarland cell suspensions per organism) from each plate.

The Xpert Carba-R Assay did not cross react with any of the organisms tested (Table 5-5, and Table 5-6). The analytical specificity of the assay was 100%.

Table 5-4: Number of Carbapenem-susceptible and Non-susceptible Organisms for each Antibiotic

	Ertapenem	Imipenem	Meropenem
Susceptible	19	30	24
Intermediate	0	8	4
Resistant	43	24	34

Table 5-5: Cross-Reactivity Panel

Organism	Strain ID	Confirmed Resistance Mechanisms	Carbapenem susceptibility (S/I/R)[a]		
			ETP[a]	IMP[a]	MEM[a]
Escherichia coli	NCTC 13441	CTX-M (15)	S	S	S
Klebsiella pneumoniae	NCTC 13465	CTX-M (25)	S	S	S
Enterobacter cloacae	Clinical isolate	OmpC/OmpF deficient	R	R	R
Citrobacter freundii	Clinical isolate	TEM (WT+164S)	S	S	S
Enterobacter cloacae	Clinical isolate	AmpC (ACT/MIR)	R	R	R
Klebsiella pneumoniae	kpn5	CTX-M-2	R	S	R
Klebsiella pneumoniae	kpn12	TEM; SHV; CTX-M	R	R	R
Escherichia coli	eco1	TEM; CTX-M-2	R	R	R
Escherichia coli	Clinical isolate	CTX-M (2); TEM	R	S	S
Enterobacter cloacae	Clinical isolate	CTX-M (2); TEM	R	R	R
Serratia marcescens	Clinical isolate	CTX-M (2); TEM	S	S	S
Morganella morganii	fer29	CTX-M (2); TEM	S	R	S
Proteus mirabilis	gut25	CTX-M (2); TEM	S	R	S
Salmonella spp.	Clinical isolate	CTX-M (2); TEM	S	S	S
Shigella flexnerii	Clinical isolate	CTX-M (2); TEM	S	S	S
Enterobacter cloacae	PA_3	AmpC; CTX-M-15; TEM	S	S	S
Klebsiella pneumoniae	Clinical isolate	SHV	S	S	S
Klebsiella pneumoniae	Clinical isolate	CTX-M (1, -type 15 like); SHV	S	S	S
Klebsiella pneumoniae	32598	CTX-M (-1, -type 15 like); SHV; TEM	R	I	R
Klebsiella pneumoniae	33560	CTX-M (15); SHV-11; TEM-1	S	S	S

Organism	Strain ID	Confirmed Resistance Mechanisms	Carbapenem susceptibility (S/I/R)[a]		
			ETP[a]	IMP[a]	MEM[a]
Klebsiella pneumoniae	33603	SHV-2	R	I	R
Klebsiella pneumoniae	Clinical isolate	SHV-27	S	S	S
Klebsiella pneumoniae	Clinical isolate	SHV (-5, -55); TEM	S	S	S
Klebsiella pneumoniae	34430	SHV; TEM; CTX-M-15	S	S	S
Klebsiella pneumoniae	34680	TEM; CTX-M-2	R	S	R
Klebsiella pneumoniae	34732	CTX-M (15); SHV; TEM	R	S	S
Enterobacter cloacae	PA_174	GX-/Culture+; SHV; TEM	S	S	S
Enterobacter aerogenes	Clinical isolate	SHV (WT+238S+240K)	R	S	R
Enterobacter aerogenes	STU 669	SHV (WT+238S+240K)	R	R	R
Escherichia coli	C3015	AmpC (CMY II); TEM	R	R	R
Enterobacter aerogenes	RI_100	AmpC (DHA); SHV	R	R	R
Klebsiella pneumoniae	B4A	SHV (WT + 238S +240K)	R	R	R
Klebsiella pneumoniae	B13A	SHV (WT + 238S +240K)	R	S	S
Enterobacter cloacae	RI_474	AmpC (ACT/MIR)	R	I	I
Enterobacter amnigenus	B71	AmpC (ACT/MIR)	R	R	R
Klebsiella pneumoniae	DD82A	SHV (WT + 238S + 240K)	R	S	R
Klebsiella pneumoniae	B100	CTX-M (-1, type-15 like); SHV (WT+238S); TEM	R	S	R
Enterobacter cloacae	135B	TEM	S	S	S
Klebsiella pneumoniae	B157	SHV; TEM	R	R	R
Escherichia coli	T2914280	CTX-M (-1, -15); TEM	R	S	R
Providencia stuartii	DD188	TEM (104K + 164S)	R	I	I
Enterobacter cloacae	DD189	AmpC (ACT/MIR)	R	S	S
Escherichia coli	B198B	CTX-M (-1, type -15 like); TEM	R	S	R
Klebsiella pneumoniae	T3019989-1	CTX-M (-1, type-15 like); SHV	R	I	R
Klebsiella pneumoniae	T3019989-2	CTX-M (-1, type-15 like); SHV	R	S	R
Enterobacter cloacae	ENC-THAI14	VEB-1, TEM	S	S	S
Escherichia coli	CB154006	CTX-M (9); TEM	R	I	I
Enterobacter cloacae	S35766	AmpC(ACT/MIR)	S	S	S
Enterobacter cloacae	X1856910	AmpC (ACT/MIR); TEM	R	I	I

Organism	Strain ID	Confirmed Resistance Mechanisms	Carbapenem susceptibility (S/I/R)[a]		
			ETP[a]	IMP[a]	MEM[a]
Klebsiella pneumoniae	W3758164	CTX-M (-1, -15 like); SHV; TEM.	R	I	R
Klebsiella pneumoniae	X2135758	CTX-M (-1, -15 like); SHV	R	S	S
Klebsiella pneumoniae	W3809535	CTX-M (-1, -15 like); SHV	R	R	R
Pseudomonas aeruginosa	CDC0064	SPM	R	R	R
Serratia marcescens	CDC0099	SME	R	R	R
Serratia marcescens	CDC0121	SME	R	R	R
Serratia marcescens	CDC0122	SME	R	R	R
Serratia marcescens	CDC0123	SME	R	R	R
Serratia marcescens	CDC0124	SME	R	R	R
Serratia marcescens	CDC0130	SME	R	R	R
Serratia marcescens	CDC0131	SME	R	R	R
Enterobacter cloacae group	CDC0132	IMI	R	R	R
Enterobacter cloacae complex	CDC0164	IMI	R	R	R

a. S/I/R = Susceptible/Intermediate/Resistant, ETP = Ertapenem, IMP = Imipenem, MEM = Meropenem

Table 5-6: Cross-reactivity Panel (Commensal and Other Enteric Microorganisms)

Organism	Strain ID
Escherichia coli	ATCC 25922
Enterococcus faecalis	ATCC 29212
Klebsiella pneumoniae	ATCC 700603
Escherichia coli	ATCC 35218
Staphylococcus aureus	ATCC 25923
Pseudomonas aeruginosa	ATCC 27853
Enterobacter cloacae	ATCC 700621
Enterococcus faecium	ATCC 9756
Klebsiella oxytoca	ATCC 13182
Acinetobacter baumannii	ATCC BAA-747
Citrobacter freundii	ATCC 33128
Morganella morganii	ATCC 49948
Stenotrophomonas maltophilia	ATCC 51331
Citrobacter koseri	ATCC 27028
Providencia stuartii	ATCC 49809
Streptococcus agalactiae	CCUG 29780 / ATCC 12401

Organism	Strain ID
Enterobacter aerogenes	ATCC 51697
Proteus mirabilis	ATCC 43071
Acinetobacter spp.	CCUG 34787
Citrobacter freundii	CCUG 418
Corynebacterium diphtheriae	CCUG 33629
Helicobacter pylori	CCUG 17874
Listeria monocytogenes	CCUG 33548
Providencia alcalifaciens	CCUG 6325

Carry-Over Contamination

A study was conducted to demonstrate that single-use, self-contained GeneXpert cartridges prevent carry-over contamination in negative samples run following very high positive samples. The study consisted of a negative sample processed in the same GeneXpert module immediately following a very high positive sample. The high positive sample is composed of inactivated *E. coli* cells containing a plasmid with an insert consisting of a synthetic oligonucleotide of the amplicon sequences from the five Xpert Carba-R target analyte genes (KPC, NDM, VIM, IMP and OXA-48 targets). Positive cells were diluted in Sample Reagent to a concentration of 1 x 10^6 CFU/mL. The testing scheme was repeated 50 times on two GeneXpert modules for a total of 102 tests (25 high positive samples per module and 26 negative samples per module). All 50 positive samples correctly reported all Xpert Carba-R targets as **DETECTED**. All 52 negative samples correctly reported all Xpert Carba-R targets as **NOT DETECTED**.

Clinical Studies

Clinical Performance

Performance characteristics of the Xpert Carba-R Assay with bacterial isolates were determined in a multi-site investigational study by comparing the Xpert Carba-R Assay to reference bi-directionalsequencing of the amplified DNA target. Study sampless included bacterial isolates grown from both blood agar and MacConkey agar.

To be included in the study, isolates must have been previously identified as *Enterobacteriaceae, Pseudomonas aeruginosa,* or *Acinetobacter baumannii*. For determination of sensitivity, isolates must have been either intermediate or resistant to meropenem, ertapenem and/or imipenem per CLSI M100-S24. Isolates of *Pseudomonas aeruginosa* or *Acinetobacter baumannii* must have been intermediate or resistant to either imipenem or meropenem. These organisms are intrinsically resistant to ertapenem. For evaluation of specificity, isolates may have been susceptible or resistant to meropenem, ertapenem, and imipenem per CLSI M100-S24. *Pseudomonas aeruginosa* and *Acinetobacter baumannii* isolates should have been susceptible to both imipenem and meropenem. Isolates were tested only once in the study.

A total of 489 isolates (431 clinical stock isolates and 58 fresh isolates) were initially enrolled in this clinical study, of which 485 were eligible for inclusion. The ineligible isolates included four isolates previously enrolled in the study.

From the 485 eligible isolates, 467 isolates (410 clinical stock isolates and 57 fresh isolates) were included in the final dataset used for the analyses presented in this report; two isolates were excluded because reference testing was not performed; and sixteen isolates were excluded because they were not identified as *Enterobacteriaceae, A. baumannii*, or *P. aeruginosa*.

For Xpert Carba-R Assay testing, well-isolated colonies that grew on each of the agar types were diluted to a 0.5 McFarland standard equivalent suspension using the direct colony suspension method per CLSI M07-A9.

For reference sequencing, DNA from culture isolates was purified, quantified, and amplified using primers specific to all 5 target genes that amplify larger regions than the assay targets and include the Xpert Carba-R primer sequences. The production of the appropriate size of amplification product was confirmed on Agilent 2100 Bioanalyzer (Agilent Technologies, Santa Clara, CA).

If bands shown on the Bioanalyzer corresponded to the expected size of the amplicon from any of the five target genes detected by the Xpert Carba-R Assay, the amplicon for the isolate was sent to an independent laboratory for reference bi-directional sequencing analysis, validated for detection of the five targets in the Xpert Carba-R Assay. If no bands were shown on the Bioanalyzer for any of the five target genes, the isolate was not sent for sequence analysis and the reference method result was considered negative for the five target genes.

Multiple targets were detected by the Xpert Carba-R Assay in samples from ten isolates. The details are provided in Table 5-7, along with the reference sequencing result.

Table 5-7. Isolates with Multiple Targets Detected

Isolate	Agar Type[a]	Targets Detected by Xpert Carba-R Assay	Targets Detected by Reference Sequencing
1	BA, MC	NDM, OXA-48	NDM, OXA-48
2	BA	VIM, KPC	VIM
3	BA, MC	NDM, OXA-48	NDM, OXA-48
4	BA, MC	NDM, OXA-48	NDM, OXA-48
5	BA, MC	NDM, OXA-48	NDM, OXA-48
6	BA, MC	NDM, OXA-48	NDM, OXA-48
7	BA, MC	NDM, OXA-48	NDM, OXA-48
8	BA, MC	NDM, OXA-48	NDM, OXA-48
9	BA, MC	NDM, OXA-48	NDM, OXA-48
10	BA, MC	NDM, OXA-48	NDM, OXA-48

a. BA=blood agar, MC=MacConkey agar

When tested with isolates from blood agar, the Xpert Carba-R Assay demonstrated an overall sensitivity and specificity of 100.0% (95% CI: 99.0-100) and 98.1% (95% CI: 93.2-99.5), respectively, relative to reference sequencing performed from the blood agar isolates (Table 5-8). The combined result was defined as positive for the Xpert Carba-R Assay if any of the targets were positive, and negative for the Xpert Carba-R Assay if all of the targets were negative.

Table 5-8: Xpert Carba-R (blood agar) vs. Reference Sequencing (isolate grown on blood agar) - Combined

Target	N	TP	FP	TN	FN	Sensitivity % (95 CI)	Specificity % (95 CI)
Overall	467	364[a]	2[a]	101	0	100.0% (99.0-100)	98.1% (93.2-99.5)

a. Combined results represent results by isolate. Multiple target results were observed for some isolates.

When tested with isolates from blood agar, the Xpert Carba-R Assay demonstrated a sensitivity and specificity of >99% for each of the five assay targets, relative to reference sequencing performed from the blood agar isolates (Table 5-9).

For isolates with discordant results between the Xpert Carba-R Assay and reference sequencing, discrepant testing was performed using bi-directional sequencing on isolates from MacConkey agar plates. Discrepant testing results are footnoted in Table 5-9 and Table 5-11.

Table 5-9: Xpert Carba-R (blood agar) vs. Reference Sequencing (isolate grown on blood agar) – By Target

Target	N	TP	FP	TN	FN	Sensitivity % (95 CI)	Specificity % (95 CI)
IMP	467	40	1[a]	426	0	100% (91.2-100)	99.8% (98.7-100)
VIM	467	82	1[b]	384	0	100% (95.5-100)	99.7% (98.5-100)
NDM	467	78	0	389	0	100% (95.3-100)	100% (99.0-100)
KPC	467	84	1[c]	382	0	100% (95.6-100)	99.7% (98.5-100)
OXA-48	467	89	0	378	0	100% (95.9-100)	100% (99.0-100)

a. The bi-directional DNA sequencing result for this false positive IMP isolate exhibited 92.95% sequence homology which was slightly below the 95% cutoff criteria. Discrepant testing was not performed.
b. Discrepant testing results: 1 of 1 was VIM positive.
c. This false positive isolate is likely due to KPC cross-contamination at the level of sample preparation. Discrepant testing did not produce a sequence match with the KPC target. Discrepant testing produced a sequence match for the VIM target, therefore this isolate is classified as a TP in the "Combined" assessment presented in Table 5-8, above.

When tested with isolates from MacConkey agar, the Xpert Carba-R Assay demonstrated an overall sensitivity and specificity of 100% (95% CI: 99.0-100) and 97.1% (95% CI: 91.8-99.0), respectively, relative to reference sequencing performed from the blood agar isolates (Table 5-10). The combined result was defined as positive for the Xpert Carba-R Assay if any of the targets were positive, and negative for the Xpert Carba-R Assay if all of the targets were negative.

Table 5-10. Xpert Carba-R (MacConkey agar) vs. Reference Sequencing (isolate grown on blood agar) – Combined

Target	N	TP	FP	TN	FN	Sensitivity % (95 CI)	Specificity % (95 CI)
Combined	467	364[a]	3	100	0	100% (99.0-100)	97.1% (91.8-99.0)

a. Combined results represent results by isolate. Multiple target results were observed for some isolates.

When tested with isolates from MacConkey agar, the Xpert Carba-R Assay demonstrated a sensitivity and specificity of >99% for each of the five assay targets, relative to reference sequencing performed from the blood agar isolates (Table 5-11).

Table 5-11. Xpert Carba-R (MacConkey agar) vs. Reference Sequencing (isolate grown on blood agar) – By Target

Target	N	TP	FP	TN	FN	Sensitivity % (95 CI)	Specificity % (95 CI)
IMP	467	40	1[a]	426	0	100% (91.2-100)	99.8% (98.7-100)
VIM	467	82	1[b]	384	0	100% (95.5-100)	99.7% (98.5-100)
NDM	467	78	1[c]	388	0	100% (95.3-100)	99.7% (98.6-100)
KPC	467	84	0	383	0	100% (95.6-100)	100% (99.0-100)
OXA-48	467	89	0	378	0	100% (95.9-100)	100% (99.0-100)

a. The bi-directional DNA sequencing result for this false positive IMP isolate exhibited 92.95% sequence homology which was slightly below the 95% cutoff criteria. Discrepant testing was not performed.
b. Discrepant testing results: 1 of 1 was VIM positive.
c. The clinical site reported that in-house characterization of this false positive isolate prior to study testing resulted in a positive NDM gene target. Discrepant testing did not produce a sequence match for any of the 5 gene targets.

The Xpert Carba-R Assay performance by specific organism group is shown in Table 5-12 for both blood agar and MacConkey Agar medium. The overall result was defined as positive for the Xpert Carba-R Assay if any of the targets were positive, and negative for the Xpert Carba-R Assay if all of the targets were negative.

Table 5-12: Xpert Carba-R vs. Reference Sequencing

Medium	Organisms	Target	N	TP	FP	TN	FN	Sensitivity% (95 CI)	Specificity% (95 CI)
Blood Agar	*Enterobacteriaceae*	IMP	343	4	0	339	0	100% (51.0-100)	100% (98.9-100)
		VIM	343	51	1	291	0	100% (93.0-100)	99.7% (98.1-99.9)
		NDM	343	73	0	270	0	100% (95.0-100)	100% (98.6-100)
		KPC	343	83	1	259	0	100% (95.6-100)	99.6% (97.9-99.9)
		OXA-48	343	89	0	254	0	100% (95.9-100)	100% (98.5-100)
		Overall	343	291[a]	1[a]	51	0	100% (98.7-100)	98.1% (89.9-99.7)
	Pseudomonas aeruginosa	IMP	80	16	1	63	0	100% (80.6-100)	98.4% (91.7-99.7)
		VIM	80	31	0	49	0	100% (89.0-100)	100% (92.7-100)
		NDM	80	0	0	80	0	NA	100% (95.4-100)
		KPC	80	1	0	79	0	100% (20.7-100)	100% (95.4-100)
		OXA-48	80	0	0	80	0	NA	100% (95.4-100)
		Overall	80	48	1	31	0	100% (92.6-100)	96.9% (84.3-99.5)
	Acinetobacter baumannii	IMP	44	20	0	24	0	100% (83.9-100)	100% (86.2-100)
		VIM	44	0	0	44	0	NA	100% (92.0-100)
		NDM	44	5	0	39	0	100% (56.6-100)	100% (91.0-100)
		KPC	44	0	0	44	0	NA	100% (92.0-100)
		OXA-48	44	0	0	44	0	NA	100% (92.0-100)
		Overall	44	25	0	19	0	100% (86.7-100)	100% (83.2-100)
MacConkey Agar	*Enterobacteriaceae*	IMP	343	4	0	339	0	100% (51.0-100)	100% (98.9-100)
		VIM	343	51	1	291	0	100% (93.0-100)	99.7% (98.1-99.9)
		NDM	343	73	1	269	0	100% (95.0-100)	99.6% (97.9-99.9)
		KPC	343	83	0	260	0	100% (95.6-100)	100% (98.5-100)
		OXA-48	343	89	0	254	0	100% (95.9-100)	100% (98.5-100)
		Overall	343	291[a]	2	50	0	100% (98.7-100)	96.2% (87.0-98.9)
	Pseudomonas aeruginosa	IMP	80	16	1	63	0	100% (80.6-100)	98.4% (91.7-99.7)
		VIM	80	31	0	49	0	100% (89.0-100)	100% (92.7-100)

Medium	Organisms	Target	N	TP	FP	TN	FN	Sensitivity% (95 CI)	Specificity% (95 CI)
		NDM	80	0	0	80	0	NA	100% (95.4-100)
		KPC	80	1	0	79	0	100% (20.7-100)	100% (95.4-100)
		OXA-48	80	0	0	80	0	NA	100% (95.4-100)
		Overall	80	48	1	31	0	100% (92.6-100)	96.9% (84.3-99.5)
	Acinetobacter baumannii	IMP	44	20	0	24	0	100% (83.9-100)	100% (86.2-100)
		VIM	44	0	0	44	0	NA	100% (92.0-100)
		NDM	44	5	0	39	0	100% (56.6-100)	100% (91.0-100)
		KPC	44	0	0	44	0	NA	100% (92.0-100)
		OXA-48	44	0	0	44	0	NA	100% (92.0-100)
		Overall	44	25	0	19	0	100% (86.7-100)	100% (83.2-100)

a.Overall results represent results by isolate. Multiple target results were observed for some isolates.

Xpert Carba-R Assay results by phenotype are presented in Table 5-13 and Table 5-14 below. Phenotypic results were based on the organism identification and susceptibility results for each of the isolates. The combined result was defined as positive for the Xpert Carba-R Assay if any of the five assay targets were positive, and negative for the Xpert Carba-R Assay if all five of the assay targets were negative. A non-susceptible phenotype means the isolate was intermediate or resistant to at least one carbapenem. A susceptible phenotype means the isolate was susceptible to imipenem, meropenem, and ertapenem.

Table 5-13. Xpert Carba-R (blood agar) vs. Phenotype – Combined

	Phenotypic Results			
Xpert Carba-R		Non-susceptible	Susceptible	Total
	Gene Detected	356	10	366
	Gene Not Detected	95	6	101
	Total	451	16	467

Table 5-14. Xpert Carba-R (MacConkey agar) vs. Phenotype – Combined

	Phenotypic Results			
Xpert Carba-R		Non-susceptible	Susceptible	Total
	Gene Detected	357	10[b]	367
	Gene Not Detected	94[a]	6	100
	Total	451	16	467

a. The 94 isolates that are phenotypically carbapenem non-susceptible but negative by the Xpert Carba-R Assay may contain other mechanisms of carbapenem resistance, such as AmpC beta-lactamases or extended spectrum beta-lactamases in combination with porin mutations, or potentially other carbapenem resistance genes that are not detected by the Xpert Carba-R Assay.

b. The 10 isolates that are phenotypically carbapenem susceptible but positive by the Xpert Carba-R assay may contain mutations that inactivate or down regulate expression of the carbapenem resistance gene detected by the Xpert Carba-R Assay.

Among the 934 tests performed (467 isolates x 2 agar types), one had an initial NO RESULT outcome (0.10%, 95% CI 0.00-0.58). The isolate yielded valid results upon repeat assay. The overall valid reporting rate of the assay was 100% (934/934).

Reproducibility Study

Reproducibility of the Xpert Carba-R Assay was evaluated using a panel of 13 bacterial samples that included: two different organisms per each of the five resistance gene targets detected by the Xpert Carba-R Assay; two stock samples that included two gene targets; and one stock sample negative for all five gene targets. Two operators at each of the three study sites tested one panel of 13 samples in replicates of four per day. Each sample was used to make two 0.5 McFarland equivalent suspensions from which two replicates were tested over six testing days (13 samples x 2 replicates x 2 times/day x 6 days x 2 operators x 3 sites). Three lots of Xpert Carba-R Assay cartridges were used at each of the 3 testing sites. The Xpert Carba-R Assay was performed according to the Xpert Carba-R Assay procedure. Upon completion of the testing, 25 tests run on one instrument module were excluded resulting in a total of 1847 samples included in the analyses. Results are summarized in Table 5-15.

Table 5-15: Summary of Reproducibility Results

Resistance Gene (Sample #)	Site 1			Site 2			Site 3			% Total Agreement by Sample
	Op 1	Op 2	Site	Op 1	Op 2	Site	Op 1	Op 2	Site	
KPC (1)	100% (24/24)	100% (24/24)	100% (48/48)	100% (24/24)	100% (24/24)	100% (48/48)	100% (24/24)	100% (24/24)	100% (48/48)	100% (144/144)
KPC (2)	100% (23/23)	100% (22/22)	100% (45/45)	95.8% (23/24)	100% (24/24)	97.9% (47/48)	100% (24/24)	100% (24/24)	100% (48/48)	99.3% (140/141)
VIM (1)	100% (22/22)	100% (23/23)	100% (45/45)	100% (24/24)	100% (24/24)	100% (48/48)	100% (24/24)	100% (24/24)	100% (48/48)	100% (141/141)
VIM (2)	100% (22/22)	100% (24/24)	100% (46/46)	100% (24/24)	100% (24/24)	100% (48/48)	100% (24/24)	100% (24/24)	100% (48/48)	100% (142/142)
IMP (1)	100% (23/23)	100% (24/24)	100% (47/47)	100% (24/24)	100% (24/24)	100% (48/48)	100% (24/24)	100% (24/24)	100% (48/48)	100% (143/143)
IMP (2)	100% (23/23)	100% (23/23)	100% (46/46)	100% (24/24)	100% (24/24)	100% (48/48)	100% (24/24)	100% (24/24)	100% (48/48)	100% (142/142)
OXA (1)	100% (23/23)	100% (23/23)	100% (46/46)	100% (24/24)	91.7% (22/24)	95.8% (46/48)	100% (24/24)	100% (24/24)	100% (48/48)	98.6% (140/142)
OXA (2)	100% (23/23)	100% (22/22)	100% (45/45)	100% (24/24)	100% (24/24)	100% (48/48)	100% (24/24)	100% (24/24)	100% (48/48)	100% (141/141)
NDM (1)	100% (22/22)	100% (21/21)	100% (43/43)	100% (24/24)	100% (24/24)	100% (48/48)	100% (24/24)	100% (24/24)	100% (48/48)	100% (139/139)
NDM (2)	100% (23/23)	100% (23/23)	100% (46/46)	91.7% (22/24)	100% (24/24)	95.8% (46/48)	100% (24/24)	100% (24/24)	100% (48/48)	98.6% (140/142)
OXA,NDM (1)	100% (24/24)	100% (23/23)	100% (47/47)	100% (24/24)	100% (24/24)	100% (48/48)	100% (24/24)	100% (24/24)	100% (48/48)	100% (143/143)
OXA,NDM (2)	100% (23/23)	100% (24/24)	100% (47/47)	100% (24/24)	100% (24/24)	100% (48/48)	100% (24/24)	100% (24/24)	100% (48/48)	100% (143/143)
NEG	100% (24/24)	100% (24/24)	100% (48/48)	100% (24/24)	100% (24/24)	100% (48/48)	100% (24/24)	100% (24/24)	100% (48/48)	100% (144/144)

The reproducibility of the Xpert Carba-R Assay was also evaluated in terms of the fluorescence signal expressed in Ct values for each target detected. The mean, standard deviation (SD), and coefficient of variation (CV) between-sites, between-lots, between-days, between-operators, and within-assays for each panel member are presented in Table 5-16.

Table 5-16. Summary of Reproducibility Data

Resistance Gene (Sample #)	Assay Channel (Analyte)	N[a]	Between-Site		Between-Lot		Between-Day		Between-Operator		Within-Assay		Total	
			SD	CV	SD	CV	SD	CV	SD	CV	SD	CV	SD	CV
KPC (1)	KPC	144	1.1	4.4	0	0	0	0	0.6	2.6	0.6	2.6	1.4	5.8
KPC (2)	KPC	143	0.8	3.1	0.1	0.2	0.2	0.9	0.5	2.0	0.8	3.1	1.2	4.9
VIM (1)	VIM	141	1.1	5.1	0	0	0	0	0.5	2.3	0.8	3.7	1.5	6.7
VIM (2)	VIM	142	0.3	1.3	0.2	0.8	0	0	0.8	3.8	0.7	3.1	1.1	5.1
IMP (1)	IMP1	143	0.3	1.0	0	0	0.3	1.2	0.6	2.3	0.8	3.1	1.0	4.2
IMP (2)	IMP1	142	1.4	6.3	0.1	0.5	0	0	0.6	2.8	0.7	3.2	1.7	7.6
OXA (1)	OXA48	140	0.6	2.6	0	0	0	0	0.7	2.8	0.8	3.5	1.2	5.2
OXA (2)	OXA48	141	1.1	4.9	0.3	1.5	0	0	0.5	2.0	0.7	3.3	1.5	6.4
NDM (1)	NDM	139	1.2	5.3	0	0	0	0	0.6	2.4	0.7	3.1	1.5	6.6
NDM (2)	NDM	140	0.9	4.0	0.3	1.4	0	0	0.8	3.3	0.8	3.3	1.5	6.3
NDM/OXA (1)	NDM	143	1.3	5.4	0.2	0.8	0	0	0.6	2.5	0.7	3.1	1.6	6.8
	OXA48	143	1.2	6.2	0.3	1.4	0	0	0.5	2.4	0.7	3.7	1.5	7.7
NDM/OXA (2)	NDM	143	1.2	5.3	0.2	1.1	0	0	0.5	2.4	0.8	3.5	1.6	6.9
	OXA48	143	1.2	6.0	0.2	1.2	0	0	0.5	2.5	0.7	3.8	1.5	7.6
NEG	SPC	144	0.1	0.3	0.1	0.3	0	0	0.2	0.5	0.4	1.3	0.5	1.5

a. Results with non-zero Ct values out of 144.

Conclusions

The results of the nonclinical analytical and clinical performance studies summarized above demonstrate that the Xpert Carba-R Assay is safe and effective for its intended use and is substantially equivalent to the predicate device.